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## What is claimed is:

1. A method for determining whether a compound is an inverse agonist of a nuclear receptor comprising the steps:

a) contacting a first polypeptide comprising a ligand binding region and a ligand dependent transactivation region of said nuclear receptor with a test compound in the presence of a second polypeptide comprising at least a receptor-binding portion of a corepressor, and

b) detecting increased binding of said first polypeptide with said second polypeptide in the presence of said compound as an indication that said test compound is an inverse agonist of said receptor.

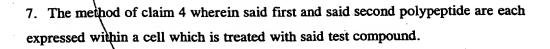
2. The method of claim 1 wherein said contacting step occurs in vivo.

3. The method of claim 2 wherein said first polypeptide and said second polypeptide each further comprise reporter elements which are directly or indirectly detectable when said first polypeptide and said second polypeptide are bound.

4. The method of claim 3 wherein the reporter element of either said first or said second polypeptide comprises a DNA binding region able to bind to a target nucleic acid, and the reporter element of the other remaining polypeptide comprises a transactivation region which will stimulate transcription of said target gene.

- 5. The method of claim 3 wherein the reporter element of either said first or said second polypeptide comprises a light-emitting moiety, and the reporter element of the remaining polypeptide comprises a moiety able to quench the emission of said light.
- 6. The method of claim 3 wherein said first and said second polypeptide are each expressed within a cell which is treated with said test compound.

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- 8. The method of either of claims 2 or 4 wherein said first polypeptide comprises a ligand binding region of a nuclear receptor selected from the group consisting of:
  - a) a retinoid receptor,
  - b) a steroid receptor,
  - c) a vitamin D receptor, and
- 10 d) a thyroid receptor.
  - 9. The method of claim 8 wherein said one of said reporter element comprises a GAL-4 transactivation region and the other said reporter element comprises a GAL-4 DNA binding region, and said contacting step occurs within a yeast cell containing a GAL-4-inducable reporter gene.
  - 10. The method of claim 8 wherein said ligand binding region is derived from a retinoid nuclear receptor.
- 20 11. The method of claim 10, wherein said ligand binding region is derived from an RAR receptor.
  - 12. The method of claim 8, wherein said ligand binding region is derived from an PPAR (peroxysome proliforator activator receptor).
  - 13. The method of claim 8 wherein said ligand binding region is derived from a thyroid receptor.
- 14. The method of claim 8 wherein said ligand binding region is derived from a vitamin D receptor.



15. The method of claim 8 wherein said ligand binding region is derived from a steroid receptor.

16. The method of claim 14 wherein said ligand binding region is derived from a steroid receptor selected from the group consisting of the estrogen receptor and the progesterone receptor.

17. The method of claim 1 wherein said contacting step occurs in vitro.

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18. The method of claim 17 wherein either said first polypeptide or said second polypeptide is labeled.

19. The method of claim 18 wherein the unlabeled polypeptide is immobilized.

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20. The method of claim 1 wherein said corepressor is selected from the group consisting of: NcoR and SMRT.

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21. A method for determining whether a compound is an inverse agonist of a nuclear receptor comprising the steps:

 a) contacting a polypeptide comprising a ligand binding region and a ligand dependent transactivation region of said nuclear receptor with a test compound in the presence of a reporter gene the expression of which is sensitive to stimulation by said nuclear receptor in the presence of an agonist of said nuclear receptor; and

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b) detecting repression of the ability of said polypeptide to stimulate expression of said reporter gene in the presence of said compound as compared to the expression of said reporter gene in the presence of said polypeptide but in the absence of a ligand of said nuclear receptor.

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- 22. The method of claim 21 wherein said nuclear receptor is selected from the group consisting of a thyroid receptor, a steroid receptor, a vitamin D receptor and a retinoid receptor.
- 5 23. The method of either of claims 21 or 22 wherein said reporter gene is integrated into the chromosome of a host cell.
  - 24. The method of either of claims 21 of 22 wherein said reporter gene is comprised in a plasmid expressed by a host cell.
  - 25. The method of claim 21 wherein/said reporter gene encodes a protein having an activity selected from the group consisting of a luciferase activity and a  $\beta$ -galactosidase activity.
- 15 26. The method of claim 23 wherein said nuclear receptor is a thyroid receptor.
  - 27. The method of claim 23 wherein said receptor is a steroid receptor.
  - 28. The method of claim 23 wherein said receptor is an estrogen receptor.
  - 29. The method of claim 23 wherein said receptor is an androgen receptor.
  - 30. The method of claim 23 wherein said receptor is an PPAR receptor.
- 25 31. The method of claim 23 wherein said receptor is a progesterone receptor.
  - 32. The method of claim 23 wherein said receptor is a vitamin D receptor.
  - 33. The method of claim 23 wherein said receptor is a retinoid receptor.

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34. The method of claim 24 wherein said nuclear receptor is a thyroid receptor.

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- 35. The method of claim 24 wherein said receptor is a steroid receptor.
- 5 36. The method of claim 24 wherein said receptor is an estrogen receptor.
  - 37. The method of claim 24 wherein said receptor is a progesterone receptor.
  - 38. The method of claim 24 wherein said receptor is a vitamin D receptor.
  - 39. The method of claim 24 wherein said receptor is a retinoid receptor.
  - 40. The method of claim 24/wherein said receptor is a androgen receptor.
- 15 41. The method of claim/24 wherein said receptor is a PPAR receptor.
  - 42. An inverse agonist identified by the method of either claim 1 or claim 18.
- 43. An inverse agonist of the RAR receptor selected from the group consisting of:
- 20 AGN 193109, AGN 193385, AGN 193389, AGN 193871 and AGN 194310.

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